Complete Summary

GUIDELINE TITLE

Treatment of DR-TB in special conditions and situations. In: Guidelines for the programmatic management of drug-resistant tuberculosis.

BIBLIOGRAPHIC SOURCE(S)

Treatment of DR-TB in special conditions and situations. In: World Health Organization (WHO). Guidelines for the programmatic management of drug-resistant tuberculosis. Geneva, Switzerland: World Health Organization (WHO); 2008. p. 79-88. [11 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Drug-resistant tuberculosis (DR-TB) in combination with:

- Pregnancy
- Breastfeeding
- Contraception
- Adolescence
- Diabetes mellitus
- Renal insufficiency
- Liver disorders
- Seizure disorders
- Psychiatric disorders

- Substance dependence

GUIDELINE CATEGORY

Evaluation
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Gastroenterology
Infectious Diseases
Internal Medicine
Nephrology
Obstetrics and Gynecology
Pediatrics
Psychiatry
Psychology

INTENDED USERS

Advanced Practice Nurses
Clinical Laboratory Personnel
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Nurses
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To outline the management of drug-resistant tuberculosis (DR-TB) in special conditions and circumstances
- To disseminate consistent, up-to-date recommendations for the diagnosis and management of multidrug-resistant tuberculosis in a variety of geographical, political, economic and social settings
- To enable access to comprehensive, up-to-date, technical and clinical information on the prevention and management of DR-TB and to encourage the implementation of known best practice
- To assist in the development of national policies to improve the diagnosis and management of DR-TB

TARGET POPULATION

Adults and children with drug-resistant tuberculosis (DR-TB) and the following conditions and situations: pregnancy, breastfeeding, use of contraception, diabetes mellitus, renal insufficiency, liver disorders, seizure disorders, psychiatric disorders, and substance abuse

Note: DR-TB in patients with human immunodeficiency virus (HIV) infection is addressed separately in the National Guideline Clearinghouse (NGC) summary of the World Health Organization (WHO) guideline, DR-TB and HIV infection.

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Initial evaluation, including pregnancy tests
2. Risk/benefit analysis of treatment
3. Monitoring of special conditions and circumstances

Treatment/Management

1. Chemotherapy treatment regimens, including first line drugs: isoniazid, rifampicin, and pyrazinamide
2. Adjustment of antituberculosis medication with consideration of the following:
    - Timing of treatment in pregnant women
    - Alternative infant formula for breastfeeding women
    - Risk of decreased efficacy of oral contraceptives
    - Timing and separation of doses of medications
    - Pediatric dosing of second-line antituberculosis drugs
    - Use of medication that makes it difficult to control insulin levels
    - Changes in dose levels of co-administered drugs
    - Renal insufficiency
    - Hepatotoxicity
    - Determination of underlying cause and degree of control of seizure disorder
    - Treatment with psychiatric medication, individual counselling, and/or group therapy for psychiatric patients
    - Treatment of substance abuse, including directly observed therapy (DOT)

MAJOR OUTCOMES CONSIDERED

- Rate of tuberculosis smear conversion
- Rate of treatment failure
- Rate of vertical transmission of tuberculosis (TB)
- Rate of exacerbation of comorbid conditions
- Rate of adverse events from therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The nominated lead author for each chapter used a limited evidence retrieval consisting of:

- Personal collection of publications and case reports
- Literatures searches using PubMed and other databases and search engines
- Existing guidelines, both from World Health Organization (WHO) and from other internationally recognized organizations
- Expert consensus during several group meetings for specific topics
- Unpublished data, for example data supplied to the Green Light Committee by their approved multidrug-resistant tuberculosis (MDR-TB) management projects

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The evidence was synthesized by each lead author, but a formal quality assessment was not used. Given the relatively small field of experts in managing drug-resistant tuberculosis, expert opinion was sought from several of the original researchers in the field. The evidence was not formally assessed or graded and there are no formal evidence summaries.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A meeting of the World Health Organization (WHO) Guidelines Steering Group, together with several WHO advisers who had contributed to the 2006 edition, took place in April 2006. It was agreed that there was an urgent need for guidance on the best response to extensively drug-resistant tuberculosis (XDR-TB), based on the emerging evidence. The group identified the chapters to be reconsidered and the gaps to be addressed in this emergency update.

Of the total 18 chapters in the original guideline document, eight have been reviewed and substantially changed in response to the emerging evidence about multidrug-resistant tuberculosis and XDR-TB (chapters 1, 4, 5, 6, 7, 10, 12 and 18). One chapter is new (Chapter 19). The remaining chapters have undergone minor revisions to ensure consistency but have not been rewritten or had any new evidence included.

There was also a decision that a full review of the Guidelines will be started after the emergency update. The WHO Guidelines Review Committee was in place by January 2008 and had already developed draft Guidance for Emergency Guidelines which was used to guide best practice in the finalization of this emergency update.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Cost is not explicitly considered as part of the recommendations, although the realities of human resources, socioeconomic issues and health system infrastructure are taken into consideration throughout the original guideline document.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The chapters were each reviewed by at least one, and usually several, members of the Guidelines Reference Group, from both within the World Health Organization (WHO) Stop tuberculosis (TB) and human immunodeficiency virus (HIV) departments and outside external experts, as appropriate. One of the expert advisers on the Steering Group was commissioned to harmonize and review all the updated chapters. The remainder of the Steering Group also reviewed the whole document and provided extensive and detailed feedback.

The first draft of the guidelines was reviewed by the Steering Group at meeting held in February 2008. Other advisers at this meeting were Dr Malgosia Grzemska

(WHO), Dr Suzanne Hill (WHO), Dr Tim Holtz (CDC, USA) and Dr Kathrin Thomas (WHO). Any outstanding issues were then resolved by e-mail to agree the final version. Other members of the group were asked to provide reviews at these later stages for particular issues.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Pregnancy

All female patients of childbearing age should be tested for pregnancy upon initial evaluation. Pregnancy is not a contraindication for treatment of active drug-resistant tuberculosis (DR-TB), which poses great risks to the lives of both mother and fetus. However, birth control is strongly recommended for all non-pregnant women receiving therapy for DR-TB because of the potential consequences for both mother and fetus resulting from frequent and severe adverse drug reactions.

Pregnant patients should be carefully evaluated, taking into consideration gestational age and severity of the DR-TB. The risks and benefits of treatment should be carefully considered, with the primary goal of smear conversion to protect the health of the mother and child, both before and after birth. The following are some general guidelines.

- **Start treatment of drug resistance in second trimester or sooner if condition of patient is severe**. Since the majority of teratogenic effects occur in the first trimester, therapy may be delayed until the second trimester. The decision to postpone the start of treatment should be agreed by both patient and doctor after analysis of the risks and benefits. It is based primarily on the clinical judgment resulting from the analysis of life-threatening signs/symptoms and severity/aggressiveness of the disease (usually reflected in extent of weight loss and lung affection during the previous weeks). When therapy is started, three or four oral drugs with demonstrated efficacy against the infecting strain should be used and then reinforced with an injectable agent and possibly other drugs immediately postpartum.
- **Avoid injectable agents**. For the most part, aminoglycosides should not be used in the regimens of pregnant patients and can be particularly toxic to the developing fetal ear. Capreomycin may also carry a risk of ototoxicity but is the injectable drug of choice if an injectable agent cannot be avoided.
- **Avoid ethionamide**. Ethionamide can increase the risk of nausea and vomiting associated with pregnancy, and teratogenic effects have been observed in animal studies. If possible, ethionamide should be avoided in pregnant patients.

Breastfeeding

A woman who is breastfeeding and has active DR-TB should receive a full course of antituberculosis treatment. Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to her baby.

In lactating mothers on treatment, most antituberculosis drugs will be found in the breast milk in concentrations that would equal only a small fraction of the therapeutic dose used in an infant. However, any effects on infants of such exposure during the full course of DR-TB treatment have not been established. Therefore, when resources and training are available, it is recommended to provide infant formula options as an alternative to breastfeeding. When infant formula is provided, fuel for boiling water and the necessary apparatus (stove, heating pans and bottles) must also be provided, as well as training on how to prepare and use the infant formula. All this should be free of charge to poor patients, and DR-TB control programmes should therefore budget in advance for the estimated number of patients who might need this support.

The mother and her baby should not be completely separated. However, if the mother is sputum smear-positive, the care of the infant should be left to family members until she becomes sputum smear-negative, if this is feasible. When the mother and infant are together, this common time should be spent in well-ventilated areas or outdoors. In some settings, the mother may be offered the option of using a surgical mask or an N-95 respirator (see the National Guideline Clearinghouse [NGC] summary of the World Health Guideline [WHO] guideline, Drug resistance and infection control) until she becomes sputum smear-negative.

Contraception

There is no contraindication to the use of oral contraceptives with the nonrifamycin containing regimens. Patients who vomit directly after taking an oral contraceptive can be at risk of decreased absorption of the drug and therefore of decreased efficacy. These patients should be advised to take their contraceptives apart from times when they may experience vomiting caused by the antituberculosis treatment. Patients who vomit at any time directly after, or within the first two hours after, taking the contraceptive tablet, should use a barrier method of contraception until a full month of the contraceptive tablets can be tolerated.

For patients with mono- and poly-resistant TB that is susceptible to rifampicin, the use of rifampicin interacts with the contraceptive drugs resulting in decreased efficacy of protection against pregnancy. A woman on oral contraception while receiving rifampicin treatment may choose between two options: following consultation with a physician, use of an oral contraceptive pill containing a higher dose of estrogen (50 micrograms); or use of another form of contraception.

Children

Children with DR-TB generally have primary resistance transmitted from an index case with DR-TB. Evaluation of children who are contacts of DR-TB patients is discussed in the NGC summary of the WHO guideline, Management of contacts of MDR-TB patients. When drug susceptibility testing (DST) is available, it should be used to guide therapy, although children with paucibacillary TB are often culture-negative. Nevertheless, every effort should be made to confirm DR-TB bacteriologically by the use of DST and to avoid exposing children unnecessarily to toxic drugs.

The treatment of culture-negative children with clinical evidence of active TB disease and contact with a documented case of DR-TB should be guided by the results of DST and the history of the contact's exposure to antituberculosis drugs (also see the NGC summary of the WHO guideline, Management of contacts of MDR-TB patients).

There is only limited reported experience with the use of second-line drugs for extended periods in children. The risks and benefits of each drug should be carefully considered in designing a regimen. Frank discussion with family members is critical, especially at the outset of therapy. DR-TB is life-threatening, and no antituberculosis drugs are absolutely contraindicated in children. Children who have received treatment for DR-TB have generally tolerated the second-line drugs well.

Although fluoroquinolones have been shown to retard cartilage development in beagle puppies, experience with the use of fluoroquinolones has not demonstrated similar effects in humans. It is considered that the benefit of fluoroquinolones in treating DR-TB in children outweighs any risk. Additionally, ethionamide, *p*-aminosalicylic acid (PAS) and cycloserine have been used effectively in children and are well tolerated.

In general, antituberculosis drugs should be dosed according to body weight (see Table 9.1 in the original guideline document). Monthly monitoring of body weight is therefore especially important in paediatric cases, with adjustment of doses as children gain weight.

All drugs, including the fluoroquinolones, should be dosed at the higher end of the recommended ranges whenever possible, except ethambutol. Ethambutol should be dosed at 15 mg/kg, and not at 25 mg/kg as sometimes used in adults with DR-TB, as it is more difficult to monitor for optic neuritis in children.

In children who are not culture-positive initially, treatment failure is difficult to assess. Persistent abnormalities on chest radiograph do not necessarily signify a lack of improvement. In children, weight loss or, more commonly, failure to gain weight adequately, is of particular concern and often one of the first (or only) signs of treatment failure. This is another key reason to monitor weight carefully in children.

Anecdotal evidence suggests that adolescents are at high risk for poor treatment outcomes. Early diagnosis, strong social support, individual and family counselling and a close relationship with the medical provider may help to improve outcomes in this group.

Diabetes Mellitus

Diabetic patients with multidrug-resistant TB (MDR-TB) are at risk for poor outcomes. In addition, the presence of diabetes mellitus may potentiate the adverse effects of antituberculosis drugs, especially renal dysfunction and peripheral neuropathy. Diabetes must be managed closely throughout the treatment of DR-TB. The health-care provider should be in close communication with the physician who manages the patient's diabetes. Oral hypoglycaemic agents are not contraindicated during the treatment of DR-TB but may require the

patient to increase the dosage. Use of ethionamide or protionamide may make it more difficult to control insulin levels. Creatinine and potassium levels should be monitored more frequently, often weekly for the first month and then at least monthly thereafter.

Renal Insufficiency

Renal insufficiency caused by longstanding TB infection itself or previous use of aminoglycosides is not uncommon. Great care should be taken in the administration of second-line drugs in patients with renal insufficiency, and the dose and/or the interval between dosing should be adjusted according to Table 9.2 in the original guideline document.

Liver Disorders

The first-line drugs isoniazid, rifampicin and pyrazinamide are all associated with hepatotoxicity. Of the three, rifampicin is least likely to cause hepatocellular damage, although it is associated with cholestatic jaundice. Pyrazinamide is the most hepatotoxic of the three first-line drugs. Among the second-line drugs, ethionamide, protionamide and PAS can also be hepatotoxic, although less so than any of the first-line drugs. Hepatitis occurs rarely with the fluoroquinolones.

Patients with a history of liver disease can receive the usual DR-TB chemotherapy regimens provided there is no clinical evidence of severe chronic liver disease, hepatitis virus carriage, recent history of acute hepatitis or excessive alcohol consumption. However, hepatotoxic reactions to antituberculosis drugs may be more common in these patients and should be anticipated.

In general, patients with chronic liver disease should not receive pyrazinamide. All other drugs can be used, but close monitoring of liver enzymes is advised. If significant aggravation of liver inflammation occurs, the drugs responsible may have to be stopped.

Uncommonly, a patient with TB may have concurrent acute hepatitis that is unrelated to TB or antituberculosis treatment. In this case, clinical judgement is necessary. In some cases, it is possible to defer antituberculosis treatment until the acute hepatitis has been resolved. In other cases when it is necessary to treat DR-TB during acute hepatitis, the combination of four nonhepatotoxic drugs is the safest option.

Seizure Disorders

Some patients requiring treatment for DR-TB will have a previous or current medical history of a seizure disorder. The first step in evaluating such patients is to determine whether the seizure disorder is under control and whether the patient is taking anti-seizure medication. If the seizures are not under control, initiation or adjustment of anti-seizure medication will be needed before the start of DR-TB therapy. In addition, any other underlying conditions or causes of seizures should be corrected.

Cycloserine should be avoided in patients with active seizure disorders that are not well controlled with medication. However, in cases where cycloserine is a crucial component of the treatment regimen, it can be given and the anti-seizure medication adjusted as needed to control the seizure disorder. The risks and benefits of using cycloserine should be discussed with the patient and the decision on whether to use cycloserine made together with the patient.

In mono- and poly-resistant cases, the use of isoniazid and rifampicin may interfere with many of the anti-seizure medications. Drug interactions should be checked before their use (see Annex 1 of the original guideline document for drug interactions).

Seizures that present for the first time during antituberculosis therapy are likely to be the result of an adverse effect of one of the antituberculosis drugs. More information on the specific strategies and protocols to address adverse effects is provided in the NGC summary of the WHO guideline, Initial evaluation, monitoring of treatment and management of adverse effects.

Psychiatric Disorders

It is advisable for psychiatric patients to be evaluated by a health-care worker with psychiatric training before the start of treatment for DR-TB. The initial evaluation documents any existing psychiatric condition and establishes a baseline for comparison if new psychiatric symptoms develop while the patient is on treatment. Any psychiatric illness identified at the start of or during treatment should be fully addressed. There is a high baseline incidence of depression and anxiety in patients with MDR-TB, often connected with the chronicity and socioeconomic stress factors related to the disease.

Treatment with psychiatric medication, individual counselling and/or group therapy may be necessary to manage the patient suffering from a psychiatric condition or an adverse psychiatric effect caused by medication. Group therapy has been very successful in providing a supportive environment for MDR-TB patients and may be helpful for patients with or without psychiatric conditions. (Adequate measures to prevent infection risk should be in place for the group therapy.)

The use of cycloserine is not absolutely contraindicated for the psychiatric patient. Adverse effects from cycloserine may be more prevalent in the psychiatric patient, but the benefits of using this drug may outweigh the potentially higher risk of adverse effects. Close monitoring is recommended if cycloserine is used in patients with psychiatric disorders.

All health-care workers treating DR-TB should work closely with a mental health specialist and have an organized system for psychiatric emergencies. Psychiatric emergencies include psychosis, suicidal ideation and any situation involving the patient's being a danger to him or herself or others. Additional information on psychiatric adverse effects is provided in the NGC summary of the WHO guideline, Initial evaluation, monitoring of treatment and management of adverse effects.

Substance Dependence

Patients with substance dependence disorders should be offered treatment for their addiction. Complete abstinence from alcohol or other substances should be strongly encouraged, although active consumption is not a contraindication for antituberculosis treatment. If the treatment is repeatedly interrupted because of the patient's dependence, therapy should be suspended until successful treatment or measures to ensure adherence have been established. Good directly observed therapy (DOT) gives the patient contact with and support from health-care providers, which often allows complete treatment even in patients with substance dependence.

Cycloserine will have a higher incidence of adverse effects (as in the psychiatric patient) in patients dependent on alcohol or other substances, including a higher incidence of seizures. However, if cycloserine is considered important to the regimen, it should be used and the patient closely observed for adverse effects, which are then adequately treated.

HIV-Infected Patients

Given the important interaction between HIV infection and drug-susceptible and DR-TB, a full guideline (see the NCG summary of WHO guideline, DR-TB and HIV infection) is devoted to this subject.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate treatment of drug-resistant tuberculosis (DR-TB) in patients with special conditions and situations

POTENTIAL HARMS

Pregnant Women

- Aminoglycosides should not be used in the regimens of pregnant patients and can be particularly toxic to the developing fetal ear.
- Capreomycin may also carry a risk of ototoxicity but is the injectable drug of choice if an injectable agent cannot be avoided.

- Ethionamide can increase the risk of nausea and vomiting associated with pregnancy, and teratogenic effects have been observed in animal studies. If possible, ethionamide should be avoided in pregnant patients.

Breastfeeding Women

- Any effects on infants of drug exposure through breast milk during the full course of drug-resistant tuberculosis (DR-TB) treatment have not been established.
- There may be a risk of infant infection while the mother is sputum-smear positive.

Contraception

The use of rifampicin may interact with contraceptive drugs, resulting in decreased efficacy of protection against pregnancy.

Children

- Although fluoroquinolones have been shown to retard cartilage development in beagle puppies, experience with the use of fluoroquinolones has not demonstrated similar effects in humans. It is considered that the benefit of fluoroquinolones in treating DR-TB in children outweighs any risk.
- Ethambutol should not be dosed at 15 mg/kg and not at 25 mg/kg as sometimes used in adults with DR-TB, as it is more difficult to monitor for optic neuritis in children.

Diabetics

Use of ethionamide or protionamide may make it more difficult to control insulin levels.

Patients with Liver Disease

Hepatotoxic reactions to antituberculosis drugs may be more common in these patients and should be anticipated.

Patients with Seizure Disorders

- Cycloserine should be avoided in patients with active seizure disorders that are not well controlled with medication.
- The use of isoniazid and rifampicin may interfere with many of the anti-seizure medications.

Patients with Psychiatric Disorders or Substance Dependence

Adverse effects from cycloserine may be more prevalent, but the benefits of using this drug may outweigh the potentially higher risk of adverse effects.

For more detailed information about adverse effects of antituberculosis drugs, see Annex 1: Drug Information Sheets, in the original guideline document.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Aminoglycosides should not be used in the regimens of pregnant patients.
- Ethionamide should be avoided in pregnant patients.
- Patients with chronic liver disease should not receive pyrazinamide.

For more detailed information about contraindications of antituberculosis drugs, see Annex 1: Drug Information Sheets, in the original guideline document.

QUALIFYING STATEMENTS

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- The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Foreign Language Translations

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Treatment of DR-TB in special conditions and situations. In: World Health Organization (WHO). Guidelines for the programmatic management of drug-resistant tuberculosis. Geneva, Switzerland: World Health Organization (WHO); 2008. p. 79-88. [11 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008

GUIDELINE DEVELOPER(S)

World Health Organization - International Agency

SOURCE(S) OF FUNDING

UK Department for International Development
United States Agency for International Development

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Steering Group

Chief Editor: Michael Rich

Editors-in-chief: Ernesto Jaramillo; Salmaan Keshavjee; Kitty Lambregts; Karen Weyer

Guidelines Reference Group

Jaime Bayona, Socios En Salud, Sucursal Peru, Lima, Peru; Jose Caminero, International Union Against Tuberculosis and Lung Disease, Paris, France; Richard Coker, London School of Hygiene and Tropical Medicine, London, UK; Charles Daley, National Jewish Medical and Research Center, Denver, CO, USA; Hamish Fraser, Partners In Health, USA; Jennifer Furin, Partners In Health, Boston, MA, USA; Giuliano Gargioni, WHO Stop TB Department, Geneva, Switzerland; Haileyesus Getahun, WHO Stop TB Department, Geneva, Switzerland; Charles Gilks, WHO HIV Department, Geneva, Switzerland; Case Gordon, World Care Council, Geneva, Switzerland; Reuben Granich, WHO HIV Department, Geneva, Switzerland; Diane Havlir, University of California, San Francisco, CA, USA; Einar Heldal, Independent consultant; Tim Holtz, United States Centers for Disease Control and Prevention, Atlanta, GA, USA; Phil Hopewell, University of California, San Francisco, CA, USA; Ernesto Jaramillo, WHO Stop TB Department, Geneva, Switzerland; Salmaan Keshavjee, Partners In Health, Harvard Medical School, Boston, MA, USA; Catharina (Kitty) Lambregts van Weezenbeek, KNCV Tuberculosis Foundation, Netherlands; Vaira Leimane, State Agency of Tuberculosis and Lung Diseases, Latvia; Refiloe Matji, University Research Corporation, South Africa; Fuad Mirzayev, WHO Stop TB Department, Geneva, Switzerland; Carole Mitnick, Harvard Medical School, Boston, MA, USA; Christo van Niekerk, Global Alliance for TB Drug Development; Domingo Palmero, Hospital Muniz, Buenos Aires, Argentina; Geneviève Pinet, WHO Legal Department, Geneva, Switzerland; Mamel Quelapio, Tropical Disease Foundation, Philippines; Michael Rich, Partners In Health/Division of Social Medicine and Health Inequalities, Brigham and Womens Hospital, Boston, MA, USA; Vija Riekstina, State Agency of Tuberculosis and Lung Diseases, Latvia; Irina Sahakyan, WHO Stop TB Department, Geneva, Switzerland; Fabio Scano, WHO Stop TB Department, Geneva, Switzerland; Adrienne Socci, Partners In Health, Boston, MA, USA; Kathrin Thomas, WHO Stop TB Department, Geneva, Switzerland; Arnaud Trébucq, International Union Against Tuberculosis and Lung Disease, Paris, France; Francis Varaine, Médecins Sans Frontières, France; Marco Vitoria, WHO HIV Department, Geneva, Switzerland; Fraser Wares, WHO Regional Office for South-East Asia, New Delhi; Karin Weyer, WHO Stop TB Department, Geneva, Switzerland; Abigail Wright, WHO Stop TB Department, Geneva, Switzerland; Matteo Zignol, WHO Stop TB Department, Geneva, Switzerland

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All of the above contributors completed a WHO Declaration of Interest form.

The following interests were declared:

Case Gordon declared that he is an unpaid advocate for patients with anti-TB drug resistance and for improved access to high-quality care. He declared that he has himself survived XDR-TB.

Tim Holtz declared that he is an unpaid technical adviser and member of the Scientific Advisory Board of a manufacturer of anti-TB products, to advise on the

development of a new anti-TB compound that will be tested in clinical trials of MDR-TB regimens.

Salmaan Keshavjee declared that his employer received funding from a foundation associated with a manufacturer of anti-TB products to support the research and training unit that he is heading.

Carole Mitnick declared that she is serving as a paid member of the Scientific Advisory Board of a manufacturer of anti-TB products, to advise on the development of a new anti-TB compound that will be tested in clinical trials of MDR-TB regimens.

Michael Rich declared that his employer received funding from a manufacturer of anti-TB products, in support of his salary.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in English, Chinese, and French in Portable Document Format (PDF) from the World Health Organization Web site.

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Executive summary. Guidelines for the programmatic management of drug-resistant tuberculosis. Geneva, Switzerland: World Health Organization (WHO); 2008. p. xi-xvi. Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization Web site.

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

In addition, various forms, registers, and reports are available in the appendices of the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on September 1, 2009. The information was verified by the guideline developer on December 11, 2009.

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